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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,740	12/24/2003	Eiichi Iishi	1422-0619P	9686
2292	7590	02/23/2006	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			HABTE, KAHSAY	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,740	IISHI ET AL.	
	Examiner	Art Unit	
	Kahsay Habte	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 January 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/3/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-5 are pending in this application.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/03/2006 has been entered.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaspersen *et al.* {Journal of Label. comp. and Radiopharm., 27, No. 9, 1055 (1989)}. Kaspersen *et al.* teaches the multi-step synthesis of Org-3770 (mirtazapine) on page 1058 (Fig.4). On page 1066, Kaspersen *et al.* also teaches the crystallization of the mirtazapine from the crude product using methanol/water solvent mixture to achieve

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almost pure crystals. Claims 1-3 are product claims, in which applicants recite some of the physical and chemical characteristics of the said product. MPEP 2112 says:

“SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DISCOVERY OF A NEW PROPERTY

The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).”

In this case, the “unknown property” is the particular crystalline form with X-ray diffraction pattern and the level of dryness. This is unknown because the reference is silent on this property. MPEP 2112 goes on to state:

“A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection.”

Again, the “CHARACTERISTIC” which the prior art is silent on is the crystalline form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound

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is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2nd 1241 at 1251.

Applicants are reminded that the PTO has no testing facilities. If applicants' reasoning were accepted, then any anticipation rejection of an old compound could always be overcome by tacking on some characteristic or property which the reference was silent on, regardless of whether the prior art material was any different from the claimed material. For example, if it did not happen to mention the color, one could patent an old compound just by adding "which is green" or "which is not indigo". One could put in a limitation about density (e.g. "density is not 1.4"), melting point, "refractive index of 2.0", solubility in some obscure solvent, spectroscopic data, and then simply point to the silence of the reference, as applicants have done here. Or one could add properties like or "does not explode on tapping" or "in the form of microneedles" or, as here, "crystals have characteristic diffraction peaks in the X-ray diffraction pattern."

Response to arguments

Applicant's argument filed 01/03/2006 has been fully considered but it is not persuasive.

Applicants argue "The present application is in the same patent family as EP 1225174 which is currently undergoing prosecution of an Opposition.....The Examiner will note that the reference 'P9' relates to van der Burg US 4,062,848 which was made of record in the December 24, 2003 IDS.....The Examiner is kindly requested to acknowledge considerations of the enclosed copy of the submission made during

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opposition at the EPO by signing and initialing the enclosed PTO/SB/08 form which lists the experimental example". Applicants further argue that "It is Applicants' position that Example 8 in the present specification is sufficiently close to the description of Kaspersen et al., so that the skilled artisan would come to the reasonable conclusion that the mirtazapine crystals of Kaspersen et al. do not have (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, as presently claimed." The examiner disagrees with applicant's conclusion. Example 8 is not the same process as the one disclosed in Kaspersen. For example, there is a pulverization step in Example 8 that is not present in Kaspersen. In addition, the drying process in Example 8 is also different from that of Kaspersen's. Thus, applicants can't rely on a disclosure that is not identical to the prior art. As argued above, applicants are speculating the outcome of a reaction. In regard to the Example 1 of foreign application EP 1225174, the experiment is not relevant to this case. Note that every case is judged on its own merit. As set forth in the previous Office Actions, applicants have to compare their compound with the prior art compound to reach such a conclusion. Note applicant's compound has passed the test (i.e. the hygroscopic degree was not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours), but this test was not done on the prior art compound.

In order to overcome this rejection, applicants have to do the test that comprise storing Kaspersen's mirtazapine crystals in the air having a relative humidity of 75% at

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25°C under atmospheric pressure for 500 hours. If the hygroscopic degree is less than 0.6% after the test, the rejection will be maintained. Applicants have to prove that the drying conditions of Kaspersen et al. would not necessarily provide mirtazapine crystals having (i) a water content of not more than 0.5% by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours. Applicants failed to address this issue that is raised in previous Office Action.

Applicants further point out to a document "Extract from Hunnius Pharmazeutisches Wörterbuch, 8th Edition, de Gruyter 1998, page 682, that discloses "Water of hydration: Water as a structural element of the crystal lattice of a substance; due to the strong fixation removal of the water of hydration is only possible by higher temperatures with destruction of crystal" and conclude that "With this knowledge of the fragility of crystals to heat, it cannot be expected that Kaspersen et al. would have used high temperatures as was used in Example 7 (90-95°C at 1330-1862 Pa) in the present specification. Certainly, if Kaspersen et al. had used temperatures, such as 90-95°C to dry the crystals, Kaspersen et al. would have described this fact in the experimental section." The examiner disagrees with applicant's conclusion. Applicants have to show this by replicating Kaspersen and present the data in declaration form. Applicants seem to predict the outcome of a reaction (e.g. drying) without actually doing the reaction.

Applicants' arguments are carefully reviewed, but the arguments are not sufficient to overcome the rejection. Note that because applicant's "special" drying

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conditions resulted in low-hygroscopic anhydrous mirtazapine crystals having (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, does not mean applicant's compound is different from the prior art compound. Applicant's compound would be different from the prior art compound (Kaspersen) if the "special" drying conditions when applied to the prior art compound gave a different property from what is claimed. This is the only way to show that applicant's compound is different from Kaspersen's compound.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

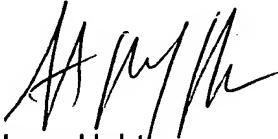
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Kahsay Habte', written in a cursive style.

Kahsay Habte
Primary Examiner
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February 20, 2006